IN THE SPECIFICATION

Please amend the specification as follows:

On page 4, please amend lines 28-31 as follows:

As an example, said first part typically has the shape of a stick, strip, paddle or plate. The shape of a ~~Nunc-Immuno™ Stick~~ NUNC-IMMUNO™ STICK *(vide infra)* is particularly preferred.

On page 5, please amend lines 3-17 as follows:

The material below the surface may be of either the same or a different material as that of the surface. The surface of said first part may thus be either completely integrated with the underlying material, i.e. said first part is made of a single type of material, or is a layer applied on virtually any kind of useful material. Preferably, the surface of the first part is that used for the surface of a ~~Nunc-Immuno™ Stick~~ NUNC-IMMUNO™ STICK. In a preferred embodiment, said first part is a ~~Nunc-Immuno™ Stick~~ NUNC-IMMUNO™ STICK, as exemplified herein below. By using the ~~Nunc-Immuno™ Stick~~ NUNC-IMMUNO™ STICK as the first part (i) mentioned above for the solid phase immunoassay according to the invention surprisingly good results are obtained. It is specially preferred due to the advantage of a rapid near-patient medical kit for monitoring drug levels in biological fluids of patients.

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On page 8, beginning with line 2 and continuing on page 9, lines 1-16, please amend the text as follows:

herein by reference.

Principle of the present invention when using the ~~Nunc immunostick~~ NUNC-IMMUNO™ STICK as the first part (i) mentioned above:

In this assay the analytes present in the biological fluid competes with the standard analyte which is immobilised on the sticks for binding with the enzyme-labelled, preferably gold-labelled, anti-analyte antibody. The procedure will be described with reference to lisinopril. The Nunc paddles are coated with the protein-lisinopril conjugate. This binds strongly by non-covalent interaction. Excess protein-drug conjugate is washed away and any free binding sites on the sticks are blocked by incubation with a protein- and detergent-containing buffer e.g., casein and ~~Tween 20~~ TWEEN-20™. After blocking, the sticks are washed in water, dried and can be stored under dry condition until further use. In the test, the sticks are placed in a tube containing a dilution of the enzyme-labelled, preferably gold-labelled, anti-lisinopril antibody and a few drops of the biological fluid being tested. After 5-10 minutes incubation to allow for the antigen-antibody reaction, the sticks are washed in tap water to remove excess labelled antibody. If the biological fluid does not have the drug, then most of the labelled antibody will bind to the drug immobilised on the sticks. This binding will reveal itself directly, in the case of gold-labelled antibody, as the gold-antibody has intense reddish colour. In the case of enzyme-labelled antibody, the binding of the antibody is revealed by the addition of a substrate (TMB in the case of horseradish peroxidase). The enzyme-labelled antibody, which is now bound to the drug immobilised on the stick, will convert the soluble substrate into

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an insoluble blue coloured product that will be deposited on the surface of the stick. The sticks are rinsed in water to remove excess substrate solution and dried. If the biological fluid contains the drug, then this will compete with the immobilised drug for binding with the antibody conjugate. This means that less antibody conjugate will bind to the drug immobilised on the sticks. Hence, the sticks will be coloured less intensely. The more free drug present in the biological fluid the less the colour intensity would be. In practice, an antibody conjugate dilution is selected that will give intense colour at or below the cut off concentration and no colour or faint colour at the "positive" concentration, e.g., for lisinopril the cut off chosen is 50 ng/ml. At this concentration or below sufficient antibody conjugate will bind to give intense colour, while at 100 ng/ml the colour intensity is faint or absent.

On page 11, please amend lines 16-19 as follows:

7. BSA is added to 10 mg/ml, ~~Tween 20~~ TWEEN-20™ to 0.05 % (w/v) and a preservative: 0.005 % thiomersal or still better 0.02 % (w/v) bromo-nitro-dioxane (BND). Aliquot are stored at -20°C.

Also on page 11, beginning at line 26 and continuing on page 12, lines 1-14, please amend the text as follows:

The interior walls of conventional microtitre wells were coated with an RSA-lisinopril conjugate by adding a solution of said conjugate (1 μg/ml; 0.1 ml) to said wells followed by incubation for 1 h at 37°C. After washing with wash buffer (10 mM sodium phosphate buffered saline, pH 7.4 containing 0.05 % sodium azide and 0.05 % ~~Tween 20~~ TWEEN-20™, PBS-T),

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250 µl/well, 3 times, the wells were incubated with varying amounts of lisinopril in human whole blood (25 µl) in the presence of HRP labelled anti-lisinopril antibody (25 ng/ml in wash buffer, 100 µl/well) for 30 min at room temperature. After washing with wash buffer the wells were incubated with the substrate, tetramethylbenzidine solution, 100 µl/well for 30 min at room temperature. Colour development was quenched by addition of 2 M sulphuric acid, 100 (µl/well and the colour intensity was measured at a wavelength of 450 nm by use of a Dynex microtitre plate reader. The results are depicted in Fig. 1. Since a lisinopril level as low as 100 pg/ml could be detected, this experiment verified that the sensitivity of the assay system of the present invention is very high.

On page 12, please amend lines 16-28 as follows:

Sticks coated with RSA-lisinopril conjugate were prepared by submerging a ~~Nunc-Immuno™ Stick~~ NUNC-IMMUNO™ STICK (manufactured by Life Technologies, UK) into a solution of RSA-lisinopril conjugate (5 µg/ml) in carbonate buffer (pH 9.5), followed by incubation for 1 h at 37°C. Phosphate buffered saline (PBS; pH 7.4) may optionally be used as solvent, and the incubation may alternatively be performed for 24 h at room temperature. After the incubation, the stick was washed in tap water and blocked in PBS containing 0.2% casein, 0.05% ~~Tween-20~~ TWEEN-20™ and 0.05% NaN_3 (preservative) for 1 h at room temperature. Then it was rinsed once in tap water, dried at room temperature and stored in a dry environment until further use thereof.

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On page 13, beginning with line 18 and continuing on page 14, lines 1-20, please amend the text as follows:

The sticks prepared as above were then inserted into tubes containing 10% (v/v) human whole blood in phosphate buffered saline (0.5 ml), containing 0.05% ~~Tween 20~~ TWEEN-20™, 0.2% casein and 10 mM EDTA (pH 7.4), as well as various concentrations of HRP labelled anti-lisinopril antibody. After incubation for 5 min at room temperature, each stick was removed, rinsed in tap water for 10 seconds and then inserted into tubes containing tetramethylbenzidine substrate for 5 minutes, after which it was rinsed as before, dried and photographed. The results are depicted in Fig. 2, and they confirm that non-specific antibody binding to the sticks is insignificant in comparison with the very high degree of specific antibody binding. A major prerequisite for the versatility of the present invention is thereby provided. For practical purposes, the most suitable colour intensity was obtained when the concentration of the HRP labelled anti-lisinopril antibody was 250 ng/ml.

Detection of lisinopril in human whole blood:

Sticks coated with RSA-lisinopril conjugate as above were submerged into a mixture (500 µl) of HRP labelled anti-lisinopril antibody (250 ng/ml; 400 µl; in phosphate buffered saline (0.5 ml), containing 0.05% ~~Tween 20~~ TWEEN-20™, 0.2% casein and 10 mM EDTA (pH 7.4)), and human whole blood (100 µl) containing various concentrations of lisinopril.

On page 15, please amend lines 16-30 as follows:

Sticks coated with either RSA-lisinopril conjugate or RSA only were prepared as described above. They were then incubated for 20 min at room temperature with gold-labelled

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rabbit anti-lisinopril antibody (200 µl; 0.2 or 0.1 optical density units/ml; in phosphate buffered saline (0.5 ml), containing 0.05% ~~Tween-20~~ TWEEN-20™, 0.2% casein and 10 mM EDTA (pH 7.4),) in the presence of human whole blood (50 µl). After the incubation the stick was removed and rinsed with tap water for 10 seconds, whereby potential colour (red) development was immediate. The results are shown in Fig. 4, and they evidence a very high binding specificity also for this system. The solution of gold-labelled rabbit anti-lisinopril antibody having an optical density of 0.2/ml was most preferred for further use.

On page 16, please amend lines 1-13 as follows:

Sticks coated with RSA-lisinopril conjugate as above were submerged into mixtures of gold-labelled rabbit anti-lisinopril antibody (200 µl; 0.2 optical density units/ml; in phosphate buffered saline (0.5 ml), containing 0.05% ~~Tween-20~~ TWEEN-20™, 0.2% casein and 10 mM EDTA (pH 7.4),) and human whole blood (50 µl) , the latter containing lisinopril at the concentrations 0, 20 and 100 ng/ml, respectively. After incubation for min, the sticks were removed and rinsed in running tap water for about 10 seconds, providing immediate colour development. The results are shown in Fig. 5, and they clearly illustrate a distinguishable colour intensity difference between the evaluated lisinopril concentrations.

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